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Undergraduate Prostate Cancer Research Project

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14. ABSTRACT: The goal of this project is to encourage undergraduates to enter careers in prostate cancer research. This project involves BCM faculty presentations at Prairie View A & M University and a 9 week summer prostate cancer research experience at BCM for 5 undergraduates/year from PVAMU (3 participated in 2006; 6 or 7 will be recruited for 2007.) Participants attended a weekly research discussion group focused on prostate cancer. Students make PowerPoint presentations on their work at the end of the program. The participants are co-registered in the SMART Program at Baylor College of Medicine ( <a href="http://www.bcm.tmc.edu/smart">www.bcm.tmc.edu/smart</a> ) and have access to elements of the SMART Program including a interdisciplinary seminar series, career development activities and career counseling and the SMART GRE Prep Course. Three students participated in the 2006 program. One student confirmed that a derivative of vitamin D reduced cell growth, one that the thyroid and estrogen receptors, but not the androgen receptor interact with a histone deacetylase. One student determined which molecules are involved in inflammation in prostate stromal cells. Student made five presentations. Participants reported significant gains in knowledge and skills. One participant was accepted by two prestigious Ph.D. programs, one is working as a technician and applying for post-bac programs to enhance her preparation for Ph.D. study and one will apply to medical school, but retains an interest in participating in prostate cancer research.					
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## **INTRODUCTION:**

The goal of this project is to encourage undergraduates to enter careers in prostate cancer research through emphasizing the importance of this health problem and generating excitement regarding opportunities to understand the disease and develop effective treatment. This project involves BCM faculty seminar presentations at Prairie View A & M University and a 9 week summer mentored prostate cancer research experience at BCM for 5 undergraduates/year from PVAMU. Students work at the forefront of research, often using high tech equipment, not typically available on undergraduate campuses. Participants attend a weekly research discussion group focused on prostate cancer that will provide opportunities to become better acquainted with prostate cancer researchers from Ph.D. students to faculty. Students make PowerPoint presentations on their work at the end of the program. The participants are co-registered in the SMART Program at Baylor College of Medicine ([www.bcm.tmc.edu/smart](http://www.bcm.tmc.edu/smart)). They have access to all elements of the SMART Program including a unique interdisciplinary seminar series, career development activities and career counseling. Participants enroll in the SMART GRE Prep Course. Social activities and dormitory housing near the Texas Medical Center will facilitate interaction with the 80-90 participants in the SMART Program who will learn about prostate cancer research from the participants funded by this proposal, amplifying the impact of the project.

## **BODY:**

Dr. Gloria Regisford organized opportunities at PVAMU for BCM faculty to present seminars, with an emphasis on prostate cancer and educational workshops at PVAMU to help recruit participants and extend knowledge of the project beyond the PVAMU students who participate in the SMART Program. Dr. Regisford has helped promote the program to individual students and provided valuable advice on working with the students. Dr. Weigel and Dr. Slaughter have presented talks and workshops at PVAMU (two times and three times since the grant was funded). Dr. Slaughter has met with PVAMU students on a field trip to BCM. Dr. Weigel arranged weekly presentations on prostate cancer for the DOD participants and any other interested SMART Program participants, minority post-baccalaureate participants, Ph.D. students, or post-docs. Typically 6-10 people attended each session. Dr. Weigel identified potential mentors and she and Dr. Slaughter matched students with mentors.

In 2006, three BCM faculty and three BCM African American Ph.D. students, two of whom are conducting prostate cancer research and one conducting breast cancer research presented seminars at PVAMU. Three PVAMU students participated in the research and educational activities of the SMART Program. They wrote abstracts and presented 20 minute talks on their research for other SMART Program participants and lab members. Two students presented posters at a PVAMU conference; one won the top research award and presented a talk at the national Annual Biomedical Research Conference for Minority Students.

One student presented a poster at a conference in Washington DC. Six PVAMU students have been recruited for the 2007 program.

We have also applied (separate from this progress report) to add two additional faculty to this program. One (Dr. Levitt) is an Assistant Professor in the Urology department with new DOD funding in prostate cancer. The second, Dr. Mims, is an MD, Ph.D. oncologist who performs clinical trials in prostate cancer and does research on polymorphisms in metabolic enzymes and risk for prostate cancer in African Americans. She has already contributed to the program by giving a lecture to the students on what is known about the biochemical basis for increased risk for prostate cancer in African Americans. These additions will increase the choices for research experiences.

### **KEY RESEARCH ACCOMPLISHMENTS:**

- Elise Copeland
  - confirmed earlier results from Dr. Nancy Weigel's lab that treating LNCaP cells with 1alpha, 25-dihydroxyvitamin D3 decreased cell number
- Theresa Okeyo-Owuor studied changes in molecules involved in inflammatory responses in prostate stromal cell lines. She
  - found that VCAM1 is not expressed in ps20 -/- cells in culture
  - ps20 and VCAM1 are over-expressed in spheroids of ps20/+ cells compared to monolayer cells
  - ps20 and IL-8 are up-regulated by LPS (induces inflammation)
  - VCAM -1 is only slightly elevated in response to LPS
- Josiah Onyenekwe
  - used RTPCR and production of recombinant protein to determine that the interaction between histone deacetylase, JHM2C, and the nuclear thyroid receptor and estrogen receptor, but not the androgen receptor, was dependent on hormone

### **REPORTABLE OUTCOMES:**

Participants reported the highest two levels of learning from lab experiences and seminars with a lower level of learning from other participants. Faculty mentors reported that all students benefited from being in the program.

Elise Copeland completed a BS degree in December, 2006 and obtained a technician position at BCM, with help from Dr. Slaughter and a supportive letter from her mentor Dr. Weigel. Elise has applied for the NIH funded SMART PREP post-baccalaureate program at BCM to better prepare herself for Ph.D. study.

Theresa was accepted for Ph.D. programs at BCM and Washington University. Her strong letter of support from her DOD mentor, Dr. David Rowley, was a major factor in gaining interviews at which Theresa distinguished herself as a top candidate. She will attend Washington University as a Ph.D. student after returning to BCM to gain further research experience through the DOD project this summer. Theresa's data will be included in a manuscript that is being prepared for publication.

Josiah Onyenekwe will complete his BS degree in August, 2007 and work as a technician while he prepares to take the MCAT and GRE exams and apply for MD/Ph.D. and DO/Ph.D, programs.

BCM faculty have participated in five seminars and workshops organized by Dr. Gloria Regisford at PVAMU since the DOD grant was awarded. African American Ph.D. students participated in seminars on cancer by Dr. Jeffrey Rosen, and two seminars on prostate cancer by Dr. Nancy Weigel. Dr. Slaughter presented a workshop on making the most of undergraduate research experiences and a workshop on preparing for the GRE for students in a 2006 summer program at PVAMU, leading to an increase in participants for the 2007 program.

Participants report that they are talking about prostate cancer to their family members, friends and classmates, more and more knowledgably. They are encouraging older family members to be screened for signs of prostate cancer. One participant discussed prostate cancer with relatives in Africa.

### Presentations

Elise Copeland, JoyAnn Phillips Rohan, Nancy Weigel. How treatment of 1,25D Inhibits Prostate Cancer Cell Growth and c-myc Gene Expression. SMART Program Research Day. July 26, 2006, Houston Texas.

Theresa Okeyo-Owuor and David Rowley. Regulation of PS20 and VCAM1 in Prostate Stroma. SMART Program Research Day. July 26, 2006, Houston TX.

Theresa Okeyo-Owuor Steve Ressler, and David Rowley. Regulation of PS20 and VCAM1 in the Prostate Stroma. Prairie View A & M University Undergraduate Research Symposium, November 3, 2006, Prairie View, TX. Won top poster award.

Theresa Okeyo-Owuor Steve Ressler, and David Rowley. Regulation of PS20 and VCAM1 in the Prostate Stroma. Selected for oral presentation at the Annual Biomedical Research Conference for Minority Students, November 10, 2006, Anaheim, CA.

Josiah Onyenekwe, Yangin Bae, Ph.D, Dr. Jiemin Wong, Ph.D The Coactivator Function of JHDM2C in T3 Mediated Transcription Activation by Thyroid Receptor. SMART Program Research Day. July 26, 2006, Houston TX.

Josiah Onyenekwe, Yangin Bae, Ph.D, Dr. Jiemin Wong, Ph.D The Coactivator Function of JHDM2C in T3 Mediated Transcription Activation by Thyroid Receptor. Prairie View A & M University Undergraduate Research Symposium, November 3, 2006, Prairie View, TX.

Josiah Onyenekwe, Yangin Bae, Ph.D, Dr. Jiemin Wong, Ph.D The Coactivator Function of JHDM2C in T3 Mediated Transcription Activation by Thyroid Receptor. SEA (Science and Engineering Alliance) Conference, Washington, DC.

#### **CONCLUSION:**

The award structure presents a challenge in terms of finding a critical mass of students specifically interested in prostate cancer research from a single campus. We only recruited three participants (five positions funded) for the first year of the program. This was, in part, due to the timing of the initial funding. We were unable to begin recruiting of students until substantially after the normal time that students begin to apply to summer programs. However, those three participants had such positive experiences that we have recruited five new participants for the 2007 program and a returning 2006 participant. The increase in participants is also due to connections created between students and BCM faculty who have presented five seminars and workshops at PVAMU since the grant was awarded.

The three 2006 participants benefited enormously from their exposure to a frontier level research environment and the seminars they attended on prostate cancer. All students gained research skills (primarily in molecular biology) and background that are helping them reach goals for advanced study. One student won a local research award and presented an excellent talk at a national conference. She raised her GRE scores and applied to three outstanding Ph.D. programs in cellular biology with a strong cancer focus. Two programs that are ranked in the top 10% in the nation accepted her with full assistantships. One student developed enough skills to improve her confidence and set a goal of entering a Ph.D. program. She is gaining further research experience and applying for a post-baccalaureate program in order to improve her preparation for graduate study. One student improved his grades in order to participate in the program, which will benefit his future application to MD/Ph.D. and DO/Ph.D. programs. He learned to read the scientific literature to understand his project and developed sufficient knowledge and confidence to ask excellent questions at the SMART Program seminars.

Theresa's acceptance by top Ph.D. programs encourages PVAMU students to set higher educational goals for themselves, and shows them what they need to

accomplish to gain opportunities at outstanding graduate schools. This partnership program has increased the presence of BCM faculty at PVAMU and enhanced the confidence of PVAMU students in interacting with senior faculty from a research intensive environment. Dr. Rosen, Dr. Slaughter and Ph.D. student Torey Batts stayed for 1 1/2 hours after the cancer seminar ended to answer questions from students about graduate education. PVAMU students are more likely to bring friends to the BCM booth at conferences to learn about our Initiative for Maximizing Student Diversity that has included more than 120 under-represented Ph.D. and MD/Ph.D. students, nearly 10 of whom have been involved in prostate cancer research.

Dr. Rowley's lab is continuing the studies Theresa began. Elise's results confirmed previous observations. Josiah's mentor is no longer at BCM or conducting prostate cancer research.

## REFERENCES

None at this time.

## APPENDIX

1. Onyenekwe J, Bae Y, Wong, J. The coactivator function of JHDM2C in T3 mediated transcription activation by thyroid receptor. Prairie View A&M University and Baylor College of Medicine/Department of Molecular and Cellular Biology.
2. Okeyo-Owuor T, Ressler S, Rowley D. Regulation of ps20 and Vcam1 in the prostate stroma. Prairie View A&M University and Baylor College of Medicine/Department of Molecular and Cellular Biology.



## **The Coactivator Function of JHDM2C in T3 Mediated Transcription Activation by Thyroid Receptor**

Josiah Onyenekwe<sup>1</sup>, Yangin Bae, Ph.D<sup>2</sup>, Dr. Jiemin Wong, Ph.D<sup>2</sup>

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Prostate cancer is the most frequently diagnosed nonskin malignancy and the second leading cause of cancer death among men right under lung cancer among men in the United States. This disease is one of the primary diseases that have been associated with somatic and germ line polymorphisms in the androgen receptor (AR) gene. AR which regulates androgen is a structurally conserved member of the nuclear receptor super family of ligand activated transcription factors. Nuclear Receptors are ligand inducible transcription factors, which regulate gene expression by interacting with DNA regulatory regions. Regulation of these genes can be associated with coactivators on the activation factors, AF-1 and AF-2. Androgen receptor (AR), part of nuclear receptor super family, has been associated with prostate cancer by demethylation associated with its ligand binding domain and activation factor 2 (AF-2). JHDM2 also called Jmjd is a family of histone demethylases with three homologs namely JHDM2A, 2B, and 2C. 2A has been found as a transcriptional activator for AR; Not much information has been found as about 2B, other than that it has been highly expressed in liver, heart, and other organs; 2C also known as TRIP8 (thyroid receptor interacting protein) shares structural similarities with 2A and requires thyroid hormone for its interaction. 2C also contains a highly conserved K9-H3 histone demethylase domain and LXXLL motif. I worked on the JHDM2C homolog with an object in investigating how 2C activates TR and nuclear dependence interactions with nuclear receptors. I did RTPCR to get a cDNA copies for the JHDM2C. Then I did GST purification as well as GST pull down to produce recombinant protein in assays to identify interactions between JHDM2C and nuclear receptors. I chose 30° C and 3hr. as the induction conditions for optimal expression. After I did the pull down assay I checked hormone dependence with of JHDM2C with three nuclear receptors namely: TR, AR, and ER (estrogen receptor), which showed that dependence with TR and ER but was unspecific with AR. This suggests that JHDM2C might not have a significant role through AR, therefore studies of coactivators for AR should focus on other molecules. The information from my study is useful because activation of TR and ER by JHDM2C may important in cancers that respond to non-androgen steroids.

O-7 Relationship Between IGFBP-3, IGF-II, and Clinical Characteristics in Breast Cancer

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**Objectives** Evidence suggests that insulin-like growth factors (IGF) may play important roles in cancer development and tumor progression. Many studies have looked at the effects that circulating IGFBP-3 and IGF-II have on normal and malignant cells. This research analyzed these two members of the IGF family in an attempt to determine any associations between their gene expression in breast tissue and the clinical characteristics of breast cancer patients. **Methods** Breast tissue samples and clinical information were collected from 236 breast cancer patients who underwent surgery. mRNA was extracted, and the expression of IGFBP-3 and IGF-II was analyzed using quantitative RT-PCR. Statistical analyses using medians and non-parametric tests were done to examine the associations between IGFBP-3 and IGF-II expression and tumor characteristics. **Results** IGFBP-3 and IGF-II expression were significantly inversely correlated to age and tumor size. Other variables did not show significant relationships. The lobular histotype had the highest expression of both IGFBP-3 and IGF-II. Expression of IGFBP-3 and IGF-II decreased with increasing tumor stage. Increasing expression of both genes was associated with increasing lymph node metastasis (pN). There were no observable trends in expression for tumor grade. **Conclusion** This study found that the expression of IGFBP-3 and IGF-II is associated with tumor size in breast cancer. This implies that their expression may be important in cell growth and proliferation. It also suggests that their expression may be useful indicators in evaluation of patients' clinical status. Funded by the NIH grant #IR25GM069997-01

MARC/MBRS/BRIDGES Program Director: Alex Randriamahefa, Ph.D.,  
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O-8 Regulation of ps20 and Vcam1 in the Prostate Stroma

Theresa Okeyo-Owuor<sup>1</sup>, Steve Ressler, Ph.D.<sup>2</sup>, David Rowley, Ph.D.<sup>2</sup>.  
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Prostate Stromal 20 (ps20) is a protein that was originally isolated from prostate stromal cells and has been characterized as a protease inhibitor. ps20 contains a WAP domain with a 4 disulphide core containing eight characteristically spaced cysteine residues. The gene encoding ps20 maps to chromosome 16q24, a region of the genome associated with copy number abnormality, loss of heterozygosity and familial association in prostate cancer. ps20 maybe involved in the upregulation of adhesion molecules and promotion of cohesion of prostate stromal cells. The aims of this project involved investigating; (1) the role of ps20 in inflammatory response; (2) the role ps20 plays in the regulation of Vcam1 in the prostate stroma. It was hypothesized that RNA levels of Vcam1 in ps20 +/- cells would be upregulated during an inflammatory response. Prostate stromal cell lines from ps20 knock out mice (ps20-/-), heterozygote mice (ps20 +/-) and a wild type (ps20 +/+) were cultured in both monolayer and spheroids for 5 days and then harvested and RNA isolated for RT-PCR. To test for regulation of ps20 and Vcam1 in inflammatory response, the cells were treated in monolayer cultures with different concentrations of LPS (Lipopolysaccharide), a pro-inflammatory inducer for 6 hours. RT-PCR was performed using primers for ps20, Vcam1, IL-8 (positive control for LPS), and GAPDH (internal control). There was an upregulation of ps20 and IL-8 during the inflammatory response induced by LPS in ps20 +/- cells but only slight upregulation of Vcam1. Vcam1 was not expressed in ps20-/- cells in culture. ps20 and Vcam-1 were over-expressed in spheroids of the ps20+/+ and ps20 +/- cells compared to monolayer cultures. These results suggest that the presence of ps20 in the stroma regulates Vcam1 expression and therefore both proteins may play a role in cohesion of the stromal cells, forming the spheroids. Inflammation has been shown to contribute in prostate disease; therefore investigating the role of ps20 in inflammation is important in the study of the growth and development of prostate cancer.